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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,200	04/22/2005	Chaim Springer	030231-0156	8842

22428 7590 07/16/2010
FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
CORNET, JEAN P	

ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
07/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,200	SPRINGER ET AL.	
	Examiner	Art Unit	
	JEAN CORNET	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-14* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/21/2010 has been entered.

Status of the claims

Claims 1-7 and 15 are canceled. Claims 8-13 are pending and under active examination. Claim 14 is withdrawn.

Rejection under *35 USC § 103*

Applicant's arguments, filed 06/21/2010, with respect to the 103(a) rejection have been fully considered and are persuasive. The rejections of 8-13 have been withdrawn due to claims amendment. Rejections and objections not reiterated form previous Office Action are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application. Applicant amended the claim to remove "…a diagnostic composition comprising microsphreres ...". The claim is now amended to recite orally administering to a subject microspheres consisting of biodegradable polymer, which is construed as the microspheres contain **only** biodegradable polymer with the exclusion of everything else.

New Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Avital et al*, **("charcoal is a Sensitive, Specific, and stable Marker for the Diagnostic of Aspiration in**

Hamsters", Pediatric Research, March 2002, pp. 397-401, Vol. 51, No. 3,) previously citd in view of *Yasuhiko et al* **"Phagocytosis of polymer microspheres by macrophages, Book, Advances in polymer Sciences, Vol. 94, ISSN 0065-3195, 1990,** *Rajeev* **"The manufacturing techniques of various drug loaded biodegradables poly(lactide-co-glycolide) (PGLA) device", Biomaterials vol. 21, 2000, pp. 2475-2490 and** *Tabata et al*, **"Macrophage phatocytosis of biodegradable microspheres composed of L-lactic acid/glycolic acid homo and copolymers", J. Biomed. Res. 1988, vol. 22, no. 10, pp. 837-858 and** *Joon et al* **(Assessment of Biodegradability of polymeric Microspheres in vivo: Poly(DL-lactic acic), and poly(L-lactic acid) and poly(DL-lactide-co-glycolide) microspheres, Arch. Pharm. Res. Vol 16, No. 4, pp. 312-317, 1193"), previously cited.**

Avitar et al. teaches a diagnostic composition for detecting aspiration by Instillation of charcoal particles in trachea of hamsters. Moreover Avitar et al teach instillation of activated charcoal particles mixed with milk was compared with instillation of normal saline or milk in hamsters and the charcoal particles were identified in bronchoalveolar lavage fluid and alveolar macrophages for a period of 3 months. In addition Avitar et al teach the charcoal particles were made from an inert non-harmful material, not produced endogenously, can be swallowed by alveolar macrophages and can be identified in alveolar macrophage for a substantial period of time and are used as a sensitive, specific and stable marker for the diagnosis of aspiration (page 397, right column). Avital et al. also teach that aspiration can occur in children with neurologic impairment, but can be secondary to gastroesophaageal reflux and the administration of the charcoal particles can be given orally (page 397, left column). Furthermore, Avital et al teaches

charcoal particles are too large and may retain within the lungs tissue for extended periods and behave as foreign bodies, inducing chronic inflammatory response and may not be safe as a diagnostic tool for humans and can cause hypercellularity (last paragraph, right column, page 400 and 401 bridging).

Avital et al does not teach a diagnostic composition comprising administering biodegradable polyester microspheres (polylactic acid) having 0.1-10 microns.

Yasuhiko et al teach that a preparation Poly (l-lactic acid) and poly (glycolic acid) copolymer resulting in poly-lactic-glycolic acid (PGLA) microspheres by solvent evaporation method. These polymers are biodegradable useful for sustained release of various drugs and targeting of therapeutic or diagnostic agent to their site of action (page 116, section 3.2.1). Moreover, Yasuhiko et al teach these microspheres are well phagocytosed by macrophages and observed by transmission electron microscope and their degradation in the cell was evaluated over time (page 134). This preparation does not involve any other ingredients but biodegradable polymer. This meets the limitation of microspheres consisting of biodegradable polymer.

Rajeev teaches PGLA is a polymer that has been widely used in humans as a biodegradable vehicle to deliver drugs and is approved by the U.S Food and Drug Administration (Abstract).

Tabata et al teach phagocitosis of PGLA microspheres with size of less than 2 microns by mouse peritoneal macrophages was studied in cell culture system using scanning electron microscopy as well as light microscopy (Abstract). Tabata et al further teach that microscopic observation clearly indicates that the phagocytosed microspheres were gradually degraded in the macrophage interior with the incubation time (Abstract).

Joon et al teach non toxic, non-tissue reactive biocompatible and biodegradable polyester microspheres such as PDLA poly(Dl-lactic acid), PLLA poly(L-lactic acid) and PLGA poly(DL-lactide-co-glycolide) selected as model polymers as noble drug carriers of various drug (page 312, second paragraph, right column). Moreover Joon et al teach 3.93 microns-5.52 microns of the PGLA microspheres were administered to mice and retained in their lungs (page 313, animal experiments). Particles ranging from 3 to 6 microns were mainly accumulated in the lungs and liver (page 314, second paragraph left column), due to their slow degradation (page 314, first paragraph, right column).

Therefore, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the charcoal particles of Avital with PGLA microspheres because the Avital et al teach charcoal particles are not safe and can be harmful to humans and cause hypercellularity in BAL, which would lead one skill in the art for a safe, inert, non harmful materials that can be identified by alveolar macrophages.

Because of the supporting properties of polyester microspheres (PGLA), the scope of the claims is embraced by the teaching of the cited references.

One would have been motivated to do so with a reasonable expectation of success to substitute the charcoal particles taught by Avital et al with polyester microspheres (PGLA) of Yasuhiko et al, Rajeev, Tabata et al and Joon et al as a sensitive and specific marker that could help diagnose aspiration, because they are safe, non-harmful, biodegradable and reliable. In addition, as demonstrated by Rajeev, these polymers have been widely used in humans and are FDA approved and they have been used as diagnostic method and are easily identified by macrophages as suggested by Yasuhiko et al and Tabata et al and lastly they have been retained

in the lungs for due to their slow degradation. Therefore, the techniques and skill required for making such substitution is conventional knowledge or well within the skill of ordinary artisan as microspheres have been used for a long time.

All the critical elements required by the claims are obvious over the well taught and thus, the claimed subject matter is not patentably distinct over the prior art of the invention.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Timothy P Thomas/

Examiner, Art Unit 1628